The translational regulator dFMRP interacts with epidermal growth factor receptor to regulate apoptosis in *Drosophila*

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Posttranscriptional gene regulation is required for all aspects of cellular and tissue development and is a major mechanism underlying many diseases ranging from neurological disorders to cancer. The translational repressor fragile x mental retardation protein (FMRP) is ubiquitously expressed throughout development but is silenced in Fragile X Syndrome, an autism spectrum disorder. Interestingly, high levels of FMRP have recently been identified in human metastatic breast cancer. FMRP overexpression in these patients is directly correlated with increased lung metastasis suggesting a direct role for translational regulation both in cell proliferation and in invasive cell migration. Interestingly, however, FMRP can promote both proliferation and apoptosis. To dissect FMRP's role in cancer development and progression, we are exploiting the powerful genetic system of *Drosophila*. *Drosophila* is an excellent model organism for human diseases associated with FMRP due to the strong evolutionary conservation of the fragile x mental retardation gene 1 which encodes this protein. dFMRP was overexpressed in the *Drosophila* imaginal wing disc, an epithelial tissue model. Contrary to a role in proliferation, overexpression of dFMRP leads to obvious cell loss in the adult wing and an increase in apoptotic markers. Using a combinatorial genetic screen, we have identified genes which are able to suppress this apoptotic phenotype and thus may be important for FMRP-dependent tumorigenesis. Our focus is now on the epidermal growth factor receptor (EGFR) signaling pathway since blocking this mechanism is able to completely rescue the dFMRP-overexpression wing defects. Clonal analysis reveals that dFMRP overexpressing cells survive their dFMRP-induced apoptotic programming when co-expressing a dominant negative form of EGFR. Additional clonal analyses are being used to explore the potential significance of this survival on tumor formation and metastasis.